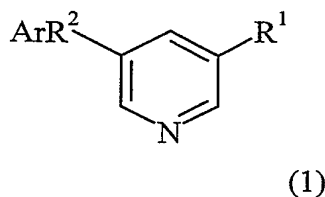


We Claim:

1. A method for treating a disorder remedied by antagonism of mGlu5 receptors in a patient which comprises administering to a patient in need thereof an effective amount of a compound of formula 1:



wherein

- Ar is phenyl or naphthyl each of which may be substituted by one or more C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>5</sub> acyl, halo, amino, nitro, cyano, hydroxy, C<sub>1</sub>-C<sub>5</sub> acylamino, C<sub>1</sub>-C<sub>4</sub> alkylsulfonylamino, mono-, di- or trifluorinated C<sub>1</sub>-C<sub>3</sub> alkyl, substituents which may be the same or different and may bear a CONH<sub>2</sub>, CONHCH<sub>3</sub>, CON(CH<sub>3</sub>)<sub>2</sub>, CO<sub>2</sub>H, CO<sub>2</sub>CH<sub>3</sub>, OCF<sub>3</sub>, CH<sub>2</sub>NHCOCH<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CN, CH<sub>2</sub>OH, CH<sub>2</sub>NHSO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>N(CH<sub>3</sub>)(CH<sub>2</sub>)<sub>2</sub> CN, CH<sub>2</sub>N(CH<sub>3</sub>)CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>NHCH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>NH(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>NHCO<sub>2</sub>R<sup>4</sup>, CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>NHCH<sub>3</sub>, NHCOC(CH<sub>3</sub>)<sub>2</sub>, or N(S(O)<sub>2</sub>CH<sub>3</sub>)<sub>2</sub> substituent;
- R<sup>1</sup> is hydrogen, halo, R<sup>4</sup>, CN, C(NOHR)<sup>3</sup>, C(NO-R<sup>4</sup>)R<sup>3</sup>, (CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>R<sup>4</sup>, (CH<sub>2</sub>)<sub>n</sub>OR<sup>3</sup>, COR<sup>3</sup>, CF<sub>3</sub>, SR<sup>4</sup>, S(O)R<sup>4</sup>, S(O)<sub>2</sub>R<sup>4</sup>, COCH<sub>2</sub>CO<sub>2</sub>R<sup>3</sup>, NHSO<sub>2</sub>R<sup>4</sup>, NHCOR<sup>3</sup>, C(NOR<sup>3</sup>)NH<sub>2</sub>, CH<sub>2</sub>OCOR<sup>3</sup>, (CH<sub>2</sub>)<sub>n</sub>NH<sub>2</sub>, CON(CH<sub>3</sub>)<sub>2</sub>, (CH<sub>2</sub>)<sub>n</sub>NHCO<sub>2</sub>R<sup>4</sup>, CO<sub>2</sub>R<sup>3</sup>, CONH<sub>2</sub>, CSNH<sub>2</sub>, C(NH)NHOR<sup>3</sup>, (CH<sub>2</sub>)<sub>n</sub>N(CH<sub>3</sub>)<sub>2</sub>, or CONHNHCOR<sup>3</sup>;
- R<sup>2</sup> is 1,2-ethenediyl or 1,2-ethynediyl;
- R<sup>3</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;
- R<sup>4</sup> is C<sub>1</sub>-C<sub>4</sub> alkyl; and
- n is 0, 1, 2, 3 or 4;
- or a pharmaceutically acceptable salt thereof; or an N-oxide thereof.

2. A method as claimed in Claim 1 wherein

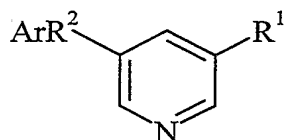
Ar is C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, C<sub>1</sub>-C<sub>5</sub>acyl, halo, amino, nitro, cyano, hydroxy, C<sub>1</sub>-C<sub>5</sub> acylamino, C<sub>1</sub>-C<sub>4</sub> alkylsulfonylamino or mono-, di- or trifluorinated C<sub>1</sub>-C<sub>3</sub> alkyl; and

R<sup>1</sup> is hydrogen, halo, R<sup>4</sup>, CN, C(NOH)R<sup>3</sup>, C(NOR<sup>4</sup>)R<sup>3</sup>, (CH)<sub>2</sub>CO<sub>2</sub>-R<sup>4</sup>, OR<sup>3</sup>, COR<sup>3</sup> or CF<sub>3</sub>.

3. The method of any one of Claims 1 or 2 wherein the disorder is pain or anxiety.

4. The method of any one of Claims 1-3 wherein the patient is a human.

5. A compound of formula 1:



(1)

wherein

Ar is phenyl or naphthyl each of which may be substituted by one or more C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>5</sub> acyl, halo, amino, nitro, cyano, hydroxy, C<sub>1</sub>-C<sub>5</sub> acylamino, C<sub>1</sub>-C<sub>4</sub> alkylsulfonylamino, mono-, di- or trifluorinated C<sub>1</sub>-C<sub>3</sub> alkyl, substituents which may be the same or different and may bear a CONH<sub>2</sub>, CONHCH<sub>3</sub>, CON(CH<sub>3</sub>)<sub>2</sub>, CO<sub>2</sub>H, CO<sub>2</sub>CH<sub>3</sub>, OCF<sub>3</sub>, CH<sub>2</sub>NHCOCH<sub>3</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CN, CH<sub>2</sub>OH, CH<sub>2</sub>NHSO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>N(CH<sub>3</sub>)(CH<sub>2</sub>)<sub>2</sub> CN, CH<sub>2</sub>N(CH<sub>3</sub>)CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>NHCH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>NH(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>NHCO<sub>2</sub>R<sup>4</sup>, CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>NHCH<sub>3</sub>, NHCOC(CH<sub>3</sub>)<sub>2</sub>, or N(S(O)<sub>2</sub>CH<sub>3</sub>)<sub>2</sub> substituent;

R<sup>1</sup> is hydrogen, halo, R<sup>4</sup>, CN, C(NOH)R<sup>3</sup>, C(NO-R<sup>4</sup>)R<sup>3</sup>, (CH)<sub>2</sub>CO<sub>2</sub>R<sup>4</sup>, (CH<sub>2</sub>)<sub>n</sub>OR<sup>3</sup>, COR<sup>3</sup>, CF<sub>3</sub>, SR<sup>4</sup>, S(O)R<sup>4</sup>, S(O)<sub>2</sub>R<sup>4</sup>, COCH<sub>2</sub>CO<sub>2</sub>R<sup>3</sup>, NHSO<sub>2</sub>R<sup>4</sup>, NHCOR<sup>3</sup>,

$C(NOR^3)NH_2$ ,  $CH_2OCOR^3$ ,  $(CH_2)_n NH_2$ ,  $CON(CH_3)_2$ ,  $(CH_2)_n NHCO_2R^4$ ,  $CO_2R^3$ ,  $CONH_2$ ,  $CSNH_2$ ,  $C(NH)NHOR^3$ ,  $(CH_2)_n N(CH_3)_2$ , or  $CONHNHCOR^3$ ;

$R^2$  is 1,2-ethenediyl or 1,2-ethynediyl;

$R^3$  is hydrogen or  $C_1$ - $C_4$  alkyl;

5  $R^4$  is  $C_1$ - $C_4$  alkyl; and

$n$  is 0, 1, 2, 3 or 4;

or a pharmaceutically acceptable salt thereof; or an N-oxide thereof; provided that the compound is other than 5-phenylethynyl-nictinonitrile.

10 6. The compound of Claim 5 wherein  $n$  is 0 or 1.

7. The compound of any one of Claims 5 or 6 wherein Ar is phenyl substituted by one or more halo,  $C_1$ - $C_4$  alkyl, CN,  $C_1$ - $C_4$  alkoxy,  $CF_3$ ,  $NO_2$ ,  $NH_2$ , OH,  $COCH_3$ , substituents which may be the same or different and may bear a  $CONH_2$ ,  
 15  $CONHCH_3$ ,  $CON(CH_3)_2$ ,  $CO_2H$ ,  $CO_2CH_3$ ,  $OCF_3$ ,  $CH_2NHCOCH_3$ ,  $CH_2NH_2$ ,  $CH_2N(CH_3)_2$ ,  $CH_2CN$ ,  $CH_2OH$ ,  $CH_2NHCH_2CH_3$ ,  $CH_2N(CH_3)(CH_2)_2 CN$ ,  $CH_2N(CH_3)CH(CH_3)_2$ ,  $CH_2NHCH(CH_3)_2$ ,  $CH_2NH(CH_2)_2CH_3$ ,  $CH_2NHCO_2C(CH_3)_3$ ,  $CH_2NHCH_2CH_3$ ,  $CH_2NHCH_3$  or  $NHCOC(CH_3)_2$  substituent.

20 8. The compound of any one of Claims 5-7 wherein halo is fluoro, iodo, choro or bromo; alkyl is methyl, ethyl, propyl, isopropyl or isobutyl; and alkoxy is methoxy.

9. The compound of any one of Claims 5-8 wherein Ar is  
 25 2-chlorophenyl, 3-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 3,4-dimethylphenyl, 3,5-dimethylphenyl, 2,4-dimethylphenyl, 2,5-dimethylphenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-chlorophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 3,4,5-trifluorophenyl,  
 30 3-bromophenyl, 3-nitrophenyl, 3-trifluoromethylphenyl, 3-aminophenyl,

3-chloro-4-fluorophenyl, 3-hydroxyphenyl, 3-acetylphenyl, 5-chloro-2-methoxyphenyl,  
 3-chloro-4-methoxyphenyl, 3-hydroxy-4-fluorophenyl, 3-methoxy-4-fluorophenyl,  
 3-ethoxy-4-fluorophenyl, 3-isopropoxy-4-fluorophenyl, 3-isopropylphenyl,  
 3-ethylphenyl, 3-methyl-4-fluorophenyl, 3-trifluoromethyl-4-fluorophenyl,  
 5 3-cyano-4-fluorophenyl, 3-amino-4-fluorophenyl,  
 3-trifluoromethyl-4-fluorophenyl, 3-chloro-4-fluorophenyl,  
 3-nitro-4-fluorophenyl, 3-aminocarbonyl-4-fluorophenyl,  
 3-N-methylaminocarbonyl-4-fluorophenyl,  
 3-N,N-dimethylaminocarbonyl-4-fluorophenyl, 3-carboxyl-4-fluorophenyl,  
 10 3-methoxycarbonyl-4-fluorophenyl, 3-acetylaminomethyl-4-fluorophenyl,  
 3-methylsulfonylaminomethyl-4-fluorophenyl,  
 3-pivaloylaminomethyl-4-fluorophenyl, 3-trifluoromethoxyphenyl,  
 3-aminomethyl-4-fluorophenyl, 3-dimethylaminomethyl-4-fluorophenyl,  
 3-cyanomethyl-4-fluorophenyl, 4-fluoro-3-hydroxymethylphenyl,  
 15 3-{[(2-cyanoethyl)-methylamino]-methyl}-4-fluorophenyl,  
 4-fluoro-3-[(isopropylmethylamino)-methyl]phenyl,  
 4-fluoro-3-isopropylaminomethylphenyl, 4-fluoro-3-propylaminomethylphenyl,  
 3-ethylaminomethyl-4-fluorophenyl, 4-fluoro-3-methyl aminomethylphenyl,  
 3-isobutyrylamino-4-fluorophenyl or 3-aminophenyl.

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10. The compound of any one of Claims 5-9 wherein  $R^1$  is hydrogen, bromo, iodo, fluoro, chloro,  $C(NO_2)R^3$ ,  $C(NO-R^4)R^3$ , methyl, CN,  $CH_2CO_2R^4$ ,  $(CH_2)_nOR^3$ ,  $COR^3$ ,  $CF_3$ ,  $SR^4$ ,  $S(O)R^4$ ,  $S(O)_2R^4$ ,  $COCH_2CO_2R^3$ ,  $NHS(O)_2R^3$ ,  $NHCOR^3$ ,  $CH_2OC(O)R^3$ ,  $(CH_2)_nNH_2$ ,  $CON(CH_3)_2$ ,  $(CH_2)_nNHCO_2R^4$ ,  $CO_2R^3$ ,  $CONH_2$ ,  $CSNH_2$ ,  $C(NH)NHOR^3$ ,  
 25  $(CH_2)_nN(CH_3)_2$  or  $CONHNHCOR^3$ .

11. The compound of any one of Claims 5-10 wherein  $R^3$  is hydrogen, methyl, ethyl or *t*-butyl.

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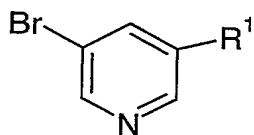
12. The compound of Claim 5 wherein  
Ar is phenyl or naphthyl each of which may be substituted by C<sub>1</sub>-C<sub>4</sub> alkyl,  
C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>5</sub> acyl, halo, amino, nitro, cyano, hydroxy, C<sub>1</sub>-C<sub>5</sub>  
acylamino, C<sub>1</sub>-C<sub>4</sub> alkylsulfonamino or mono-, di- or trifluorinated C<sub>1</sub>-C<sub>3</sub>  
alkyl; and  
R<sup>1</sup> is hydrogen, halo, R<sup>4</sup>, CN, C(NO<sub>2</sub>)R<sup>3</sup>, C(NOR<sup>4</sup>)R<sup>3</sup>  
(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>R<sup>4</sup>, OR<sup>3</sup>, COR<sup>3</sup> or CF<sub>3</sub>.
13. The compound of formula I as claimed in any one of Claims 5-12 wherein  
R<sup>1</sup> is CN, iodo, chloro, methyl or COR<sup>3</sup>.
14. The compound of formula I as claimed in any one of Claims 5-13 wherein  
R<sup>1</sup> is CN.
15. The compound of formula I as claimed in any one of Claims 5-14 wherein  
R<sup>2</sup> is 1,2-ethynediyl.
16. The compound of formula 1 as claimed in any one of Claims 5-15 wherein  
C<sub>1</sub>-C<sub>4</sub> alkyl is methyl.
17. The compound of formula 1 as claimed in any one of Claims 5-16 wherein  
R<sup>3</sup> is methyl.
18. A compound of formula 1 as claimed in any one of a Claims 5-16 wherein  
R<sup>3</sup> is hydrogen.
19. The compound of any one of Claims 5-18 wherein substituted Ar is  
substituted phenyl.
20. The compound of any one of Claims 5-6, 8 or 10-18 wherein Ar is phenyl.

21. A compound of claim 5 which is:

5-(4-Fluorophenylethynyl)-nicotinonitrile, 5-(3-Cyanophenylethynyl)-nicotinonitrile or 5-(3,4-difluorophenylethynyl)-nicotinonitrile.

22. A process for preparing a compound of formula 1 (or a pharmaceutically acceptable salt thereof) as provided in any one of the above Claims 5-21 which comprises:

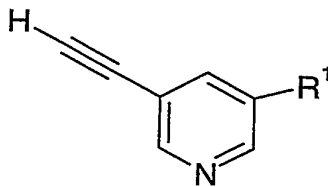
(a) for a compound of formula 1 in which  $R^2$  is 1,2-ethenediyl, reacting with a compound of formula II



(II)

with a compound of formula  $Ar-CHCH_2$  in a Heck coupling;

(b) for a compound of formula 1 in which  $R^2$  is alkynyl, reacting with a compound of formula III



(III)

in a Sonogashira coupling with a compound of formula  $Ar-I$  or  $Ar-Br$  in a suitable solvent;

whereafter, for any of the above procedures, when a pharmaceutically acceptable salt of a compound of formula 1 is required, it is obtained by reacting the basic form of such a compound of formula 1 with an acid affording a physiologically acceptable

counterion, or, for a compound of formula 1 which bears an acidic moiety, reacting the acidic form of such a compound of formula 1 with a base which affords a pharmaceutically acceptable cation, or by any other conventional procedure; and wherein, unless more specifically described, the value of R<sup>1</sup>, Ar and R<sup>2</sup> are as defined in Claim 5.

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23. A pharmaceutical composition comprising in association with a pharmaceutically acceptable carrier, diluent or excipient, a compound of formula 1 (or a pharmaceutically acceptable salt thereof) as provided in any one of the above Claims 5-21.

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24. A compound of formula 1 as claimed in Claim 1 for use in therapy.

25. Use of compound of formula 1 as claimed in Claim 1 for the manufacture of a medicament for treating a disorder remedied by antagonism of mGlu5 receptors in a patient.

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